

August 11, 2005

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Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Docket Number 2005P-0520 (Citizen Petition) – Third Submission of
Comments by IVAX Pharmaceuticals

Dear Sir or Madam:

These comments are submitted on behalf of IVAX Pharmaceuticals, Inc., (IVAX) in response to a third submission of comments by Eon Labs dated July 11, 2005, regarding the Citizen Petition filed by IVAX on November 19, 2005.¹

BACKGROUND

This matter involves a determination of 180-day exclusivity under a limited and unique set of circumstances. Both IVAX and Eon submitted their ANDAs prior to passage of the MMA and both ANDAs are subject to the MMA provisions governing notice requirements for paragraph IV certifications.² Because IVAX submitted its ANDA prior to the listing of the patent at issue, IVAX is subject to the MMA provisions governing 30-month stays and, in this case, is not subject to a thirty month stay.³ Eon, however, may be subject to a thirty month stay because it filed its ANDA after the Dey patent was listed. Neither IVAX nor Eon are subject to the MMA provisions on 180-day exclusivity because the first paragraph IV certification was submitted (by IVAX) prior to the passage of the MMA.⁴ Thus we have a unique situation in which the agency must

¹ Docket No. 2005P-0520: P1 (Nov. 19, 2004).

² The notice provisions of the MMA § 1101(c)(2) apply to applications pending at the time of passage of the MMA if the applications contain paragraph IV certifications submitted on or after August 18, 2003. Both IVAX and Eon submitted their certifications after that date.

³ See MMA § 1101(c)(3).

⁴ See MMA § 1102(b)(1). The pre-MMA exclusivity provisions provide as follows:

If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after -

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.

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determine eligibility for exclusivity between two ANDAs that (1) are subject to the pre-MMA exclusivity provisions, (2) are subject to the MMA notice provisions, and (3) are each subject to differing provisions regarding 30-month stays.

IVAX's position is that, under these circumstances, eligibility for 180-day exclusivity (first filer status) must be determined based on the dates that IVAX and Eon satisfied the MMA notice requirement associated with the submission of their paragraph IV certifications. Had the MMA exclusivity provisions been applicable to IVAX's ANDA, the wording of the statute would have dictated this result because Congress provided an express enforcement provision for the MMA notice requirements in the definition of "first applicant," which directs that exclusivity be determined based not on the date of physical submission of the paragraph IV certification but rather on the date that FDA determines that the certification was both submitted and "lawfully maintain[ed]."⁶ Here, however, the MMA exclusivity provisions are inapplicable and the MMA notice provisions must be enforced under the pre-MMA exclusivity provisions. The outcome, nevertheless, is the same.

Under the agency's interpretation of the pre-MMA exclusivity provisions, exclusivity eligibility determinations must be based on the date of notice associated with submission of the paragraph IV certification where the statute requires notice by a date certain.⁷ Because the pre-MMA notice provisions required notice by a date certain only

Formerly FDCA § 505(j)(5)(B)(iv).

⁶ Under the MMA, an ANDA applicant submitting a paragraph IV certification is required to maintain its certification by providing notice to the patent holder by a date certain. FDCA § 505(j)(2)(B)(i), (ii). The MMA provides an express enforcement mechanism for these notice requirements by defining 180-day exclusivity as a delay that would apply to an ANDA "submitted by an applicant other than a first applicant," and by defining a "first applicant" as an applicant that "submits a substantially complete application that contains *and lawfully maintains* a [paragraph IV] certification" on the first day that any applicant submits such a certification. FDCA § 505(j)(5)(B)(iv)(II)(aa), (bb). Thus an applicant cannot qualify as a first applicant until the applicant satisfies the requirement that the paragraph IV certification be lawfully maintained by satisfaction of the notice requirement. Because there is no other duty placed on an ANDA applicant with regard to a paragraph IV certification, the date of satisfaction of the notice requirement provides the date upon which the applicant has satisfied the requirement that the certification be lawfully maintained.

⁷ The agency's pre-MMA policy grew out of the agency's experience with ANDA applicants that failed to heed the express statutory mandate that, where a paragraph IV certification is submitted in an ANDA amendment, the applicant provide the notice on the date that the amendment is submitted. The courts have agreed with FDA's approach because (1) the statute provided a mandate that the notice be provided by a date certain, (2) the statute provided no express enforcement mechanism for the notice requirement, and (3) FDA fashioned a reasonable enforcement mechanism by determining eligibility for exclusivity based on the date of compliance with the notice requirement. *Purepac v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004), *aff'g TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69, 79-81 (D.D.C. 2003). The alternative enforcement mechanism suggested under the pre-MMA statute, nullification of the paragraph IV certification, was rejected by FDA and properly considered "draconian" by one district court. *TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d at 81.

for ANDA amendments, the agency did not determine exclusivity based on date of notice for original ANDAs that were subject to pre-MMA notice provisions. With the modification of the notice provisions under the MMA to require notice by a date certain for both original ANDAs and ANDA amendments,⁸ the agency's interpretation of the pre-MMA exclusivity provisions requires in the context of MMA notice provisions that exclusivity be determined based on the date of notice for both original ANDAs and ANDA amendments.

EON'S COMMENTS

Eon's most recent comments, like its previous submissions of comments, largely argue (1) that IVAX has misinterpreted the MMA *exclusivity* provisions and (2) that FDA should change its interpretation of the pre-MMA exclusivity provisions and determine exclusivity eligibility based on date of physical submission of Eon's paragraph IV certification even though the MMA notice provisions required both Eon and IVAX to provide notice by a date certain. In considering Eon's comments it is important to keep four points in mind:

1. **The resolution of this matter does not involve application of the 180-day exclusivity provisions of the MMA and does not necessarily require their interpretation.** Those provisions are relevant only insofar as make clear that Congress intended the MMA *notice* provisions to be enforced through the MMA exclusivity provisions. Congress did not expressly address the unique situation in which the MMA notice provisions would have to be enforced through the pre-MMA exclusivity provisions.
2. **The agency should resolve this matter based on its interpretation of the pre-MMA 180-day exclusivity provisions.** The agency has heretofore interpreted those provisions to require a determination of eligibility based on satisfaction of the statutory notice requirement where notice must be provided by a date certain. Under this interpretation the agency must award exclusivity to IVAX because the MMA notice provisions require notice by a date certain for both original ANDAs and for ANDA amendments..
3. **Eon has offered no legally supportable basis for its proposed change in the agency's interpretation.** Eon's sole argument is that exclusivity should be determined based on date of submission for original ANDAs because that would have been the outcome under the agency's application of the pre-MMA notice provisions. Although

⁸ Under the MMA, Congress eliminated the distinction between original ANDAs and ANDA amendments, providing that for each submission the applicant not only shall provide a statement that the applicant will give notice, FDCA § 505(j)(2)(B)(i),⁸ but also "*shall give notice* as required under this subparagraph."⁸ *Id.* § 505(j)(2)(B)(ii) (emphasis added).

¹⁰ See *Weinberger v. Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609, 631-32 (1973) ("It is well established that our task in interpreting separate provisions of a single Act is to give the Act "the most harmonious, comprehensive meaning possible" in light of the legislative policy and purpose) (citations omitted).

Eon characterizes this outcome as an “interpretation,” it is not. To the extent that this outcome reflects an interpretation of the statute, it reflects an interpretation of the interplay between statutory provisions (pre-MMA exclusivity provisions and pre-MMA notice provisions) that are not applicable here, where instead the agency must interpret the interplay between pre-MMA exclusivity provisions and MMA notice provisions.

4. Even if the agency were to consider developing a new interpretation of the pre-MMA exclusivity provisions (an interpretation that would not require enforcement of statutory notice-by-date-certain requirements), there is no reasonable interpretation of the statute under which Eon can be granted exclusivity.

Any new interpretation would have to accommodate reasonably the MMA provisions related to notice and 30-month stays that are applicable to IVAX’s ANDA.¹⁰ The agency cannot accommodate those provisions under any new interpretation of the statute that would establish different rules for original ANDAs and ANDA amendments so as to award exclusivity to a Johnny-come-lately ANDA and derail the approval of a pending ANDA filed before the patent was listed. To survive judicial challenge in the unique circumstances presented in this matter, any new interpretation would have to resolve exclusivity eligibility *between a pending ANDA and a later-filed original ANDA* consistent with Congress’ broader statutory intent under the applicable MMA provisions.

When Congress removed the distinction between original ANDAs and ANDA amendments in the MMA notice provisions by requiring for each that notice be provided by a date certain, Congress eliminated any statutory rationale for a distinction between original ANDAs and ANDA amendments for purposes of determining exclusivity based on statutory notice requirements. In fact, the wording of the MMA provisions suggests a presumption that the notice provisions should be enforced in the same manner for both types of submissions.

The new MMA provisions on 30-month stays further undermine Eon’s proposed interpretation by evidencing a strong congressional intent that that later-filed ANDAs (filed after listing of a patent) not be given an advantage over pending ANDAs that must be amended based on later-filed patents. As noted in IVAX’s petition, one of the key

¹² As discussed in IVAX’s petition, the legislative history reveals that FDA, FTC, and Congress were all concerned over this problem. The FTC conducted a study and provided recommendations related to delays in generic drug approval resulting from the patent listing process, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* (2002) (FTC Report), that played a central role in passage of the MMA. See *Hearing Before the Senate Judiciary Comm. on the Senate and House Versions of the "Greater Access to Affordable Pharmaceuticals Act,"* 108th Cong. (2003) (remarks of Senator Hatch) (“The one and only 30-month stay for all patents filed when the ANDA was submitted was also a centerpiece of the Federal Trade Commission report issued last summer.”); *id.*, (testimony of Dan Troy, Chief Counsel, FDA) (“Both the Senate and the House bills amend Hatch-Waxman to allow only one 30-month stay per drug product, per ANDA for patents listed in the Orange Book prior to the generic company filing its ANDA. The FTC Study recommended this exact change.”). The FTC Report, cited in the legislative history, makes clear that the recommendation that 30-month stays be eliminated for patents listed during the review of an ANDA was based in part on the concern that such stays might delay the ANDA approval significantly beyond the normal review period. FTC Report at iv

purposes of the MMA amendments to the FDCA was to eliminate 30-month stays in the approval of an ANDA based on the listing of a patent during the agency's review of the ANDA. Should the agency determine first applicant status for Eon's later-filed ANDA based on date of submission of its ANDA but determine first applicant status for IVAX based on date of notice, Eon would enjoy an unfair advantage over IVAX, which submitted its ANDA well prior to the listing of the patent. This would be contrary to the clear intent behind the 30-month stay provisions to protect pending ANDAs from delays in approval based on patent listings during the review of the ANDA that might result in 30-month stays.¹²

It would also pose a potential paradox that would clearly contravene the intent of Congress. Dey (the NDA holder) has taken the position in a citizen petition that Eon's ANDA is subject to the 30-month stay because it was submitted after the listing of the patent.¹³ Dey has also submitted an amendment to its petition that supports Eon's status as a first applicant in its effort to prevent imminent final agency action on IVAX's ANDA. Eon's proposed interpretation would thus not only award Eon 180-day exclusivity on the eve of completion of FDA's review of the IVAX ANDA, but would also block approval of IVAX's ANDA *during the 30-month stay* resulting from a patent lawsuit filed against Eon should the agency grant Dey's petition. It would essentially impose a 30-month stay on IVAX's ANDA, based on a later-listed patent, that would delay approval of the ANDA beyond the normal review cycle.

To avoid this outcome, FDA must interpret the pre-MMA exclusivity provisions in a manner that will avoid favoring a later-filed ANDA over a pending ANDA that was filed before a patent was listed.

Should the agency abandon its interpretation of the pre-MMA exclusivity provisions, it might in theory be possible to formulate a new, narrower interpretation of those provisions that would advance the statutory objectives of the MMA notice and 30-month stay provisions by determining exclusivity based on date of notice *where at least one ANDA was submitted prior to submission of the patent*. This outcome would accommodate the new notice and 30-month stay provisions that are applicable to IVAX's ANDA in the unusual circumstances presented here where both MMA and pre-MMA provisions apply, and would avoid judicial challenge by IVAX.

For the reasons stated in IVAX's petition, however, the agency's current interpretation, which would result in an award of exclusivity to IVAX based on date of

¹³ Amendment to Citizen Petition, Docket No. 2004P-0324-AMD1 (August 30, 2004). In the petition amendment, Dey argues that Eon is subject to a 30-month stay because, according to Dey, Eon submitted its ANDA subsequent to the listing of the patent. *Id.* at 3.

notice, is consistent with the legislative intent behind the MMA 30-month stay and notice provisions and should be retained by the agency.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "David G. Adams", written over a horizontal line.

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August 11, 2005

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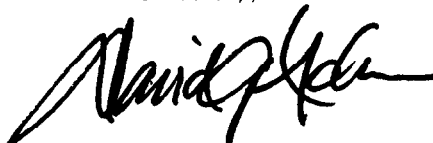
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Dear Sir or Madam:

Please accept the attached comments (in four copies) submitted on behalf of
IVAX Pharmaceuticals, Inc., pursuant to 21 C.F.R. § 10.35.

Sincerely,



David G. Adams